Dextran sulfate

Drug Class: **Microbicides**

Drug Description

Dextran sulfate, also known as DS, is a heparin-like long-chain polysaccharide containing approximately 17% sulfur and up to three sulfate groups per glucose molecule. [1] [2]

HIV/AIDS-Related Uses

Dextran sulfate, an investigational drug, was previously studied for use as a potent inhibitor of HIV-1. Toxic adverse effects, including profound thrombocytopenia, prevented further in vivo research.[3]

Recent Phase I/II clinical studies have confirmed the safety and acceptability of dextran sulfate as a vaginal microbicide.[4] Dextran sulfate is now being evaluated as a microbicide to prevent the sexual transmission of HIV-1.[5]

Non-HIV/AIDS-Related Uses

Dextran sulfate is an anticoagulant and antihyperlipidemic agent.[6] Dextran sulfate has also been evaluated in vitro and in vivo as a microbicide inhibitor of herpes simplex virus (HSV)-1, HSV-2, and human papillomaviruses.[7]

Pharmacology

Dextran sulfate and other sulfated polysaccharides are potent and selective inhibitors of HIV-1 CXCR4 isolates.[8] Experiments carried out with dextran sulfate samples of increasing molecular weight and degree of sulfation have shown that antiviral activity increases with increasing molecular weight and degree of sulfation.[9]

Sulfated carbohydrates like dextran sulfate exert their inhibitory HIV effects by interacting with the positively charged amino acids in the V3 loop of the viral envelope glycoprotein gp120.[10] This interaction prevents viral attachment to the cell surface and the interaction between gp120 and the CD4 receptor on T cells.[11] [12]

Binding of gp120 varies depending on the isolate and may reflect the type of saccharide residues and the degree and positions of sulfation. Molar percent inhibition differences seen between various sulfated compounds suggest a specific or preferential interaction rather than simple, nonspecific, negatively-charged sulfate interactions with the V3 loop.[13]

Sulfated carbohydrates show activity against HIV mutants that have become resistant to nucleoside reverse transcriptase inhibitors such as zidovudine, and they appear to develop drug resistance very slowly.[14]

HIV resistance to polysulfated carbohydrates may be mapped to single amino acid changes, including those outside the V3 loop region. In one resistance study, a single mutation located in the V2 loop of gp120, K178E, induced a 48-fold change in sensitivity to dextran sulfate. A single amino acid change at position 322 in the V3 loop (K322Q) conferred 62-fold virus resistance to dextran sulfate. These changes did not alter HIV-1 sensitivity to CXCR4 ligands, the fusion inhibitor enfuvirtide, or zidovudine. A previously found dextran sulfate mutation, Q310H, did not confer a change in virus sensitivity. This suggests that Q310H is not relevant for direct resistance but may be needed to facilitate the emergence of drug-resistant mutations.[15]

Dextran sulfate and other sulfated carbohydrates may inhibit HSV through competitive inhibition for binding to glycosaminoglycans on the host cell surface.[16]

Adverse Events/Toxicity

Continuous IV infusion of dextran sulfate is toxic, producing profound but reversible thrombocytopenia and extensive but reversible alopecia. Because of its toxicity, IV dextran sulfate is no longer studied for use in treating HIV.[17]

Intravaginal gel use of the drug is associated with minor adverse effects in clinical trials. Increased thirst and unexplained intermenstrual bleeding were observed but were not considered severe.[18] [19] No evidence of systemic toxicity or genital irritation was associated with twice daily gel use in

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Adverse Events/Toxicity (cont.)

HIV infected and uninfected women.[20] In a four-week study of gel acceptability when applied twice-daily or just prior to sexual activity, nearly all women using dextran sulfate said they would continue using or recommend use of the gel. Side effects associated with twice-daily use included itching, irritation, bleeding, slippery feeling, and a cold feeling. Women also complained of the gel interfering with sex due to excess lubrication and the need to apply the gel too frequently.[21] No differences were noted between women using 1% dextran sulfate gel compared to those using 4% gel.[22]

Drug and Food Interactions

Sulfated polysaccharides such as dextran sulfate may act synergistically with other anti-HIV drugs (e.g., zidovudine).[23]

Clinical Trials

For information on clinical trials that involve Dextran sulfate, visit the ClinicalTrials.gov web site at http://www.clinicaltrials.gov. In the Search box, enter: Dextran sulfate AND HIV Infections.

Dosing Information

Mode of Delivery: Intravaginal.[24]

Dosage Form: Intravaginal gel administered twice daily or just prior to sexual activity.[25] [26] Clinical trials have evaluated concentrations of 1% or 4% gel.[27]

Chemistry

CAS Name: Dextran, hydrogen sulfate[28]

CAS Number: 9042-14-2[29]

Molecular formula: H2-O4-S.x-Unspecified[30]

Molecular composition: 17% to 20% sulfur content[31]

Molecular weight: 4,000 to 500,000 daltons[32]

Physical Description: White powder from alcohol plus ether.[33]

Solubility: Freely soluble in water.[34]

Other Names

DS[35]

Dextran sulfate sodium[36]

Dextrin sulphate[37]

DxS[38]

Dextrin sulfate[39]

Further Reading

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Manufacturer Information

Dextran sulfate
Ueno Fine Chemicals Industry Ltd
1133 Sixth Ave / 27th Floor
New York, NY 10036
(212) 935-2323

For More Information

Contact your doctor or an AIDSinfo Health Information Specialist:

• Via Phone: 1-800-448-0440 Monday - Friday, 12:00 p.m. (Noon) - 5:00 p.m. ET

• Via Live Help: http://aidsinfo.nih.gov/live_help Monday - Friday, 12:00 p.m. (Noon) - 4:00 p.m. ET

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